

# Turner syndrome

## Relation between genotype and phenotype and long-term follow-up studies

Akademisk avhandling

Som för avläggande av doktorsexamen i medicinsk vetenskap vid Sahlgrenska Akademien vid Göteborgs Universitet kommer att offentligen försvaras på Academicum, Arvid Carlssons föreläsningssal, Medicinaregatan 3, Göteborg, fredagen den 20 november 2009, kl 9.00

av

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Avhandlingen baseras på följande arbeten:

**I** El-Mansoury M, Barrenäs M-L, Bryman I, Hanson C, Larsson C, Wilhelmsen L, Landin-Wilhelmsen K. **Chromosomal mosaicism mitigates stigmata and cardiovascular risk factors in Turner syndrome.**

*Clinical Endocrinology* 2007;66:744-51.

**II** El-Mansoury M, Barrenäs M-L, Bryman I, Hanson C, Landin-Wilhelmsen K. **Impaired body balance, fine motor function and hearing in women with Turner syndrome.**

*Clinical Endocrinology*; 2009;71:273-8.

**III** El-Mansoury M, Bryman I, Berntorp K, Hanson C, Wilhelmsen L, Landin-Wilhelmsen K. **Hypothyroidism is common in Turner syndrome – results from a five-year follow-up.**

*Journal of Clinical Endocrinology and Metabolism*, 2005;90:2131-2135.

**IV** El-Mansoury M, Berntorp K, Bryman I, Hanson C, Innala E, Karlsson A, Landin-Wilhelmsen K. **Elevated liver enzymes in Turner syndrome during a 5-year follow-up study.**

*Clinical Endocrinology* 2008;68:485-90.

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## **Abstract**

### **Turner syndrome - Relation between genotype and phenotype and long-term follow-up studies**

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Turner syndrome (TS) is a chromosomal disorder with a prevalence of approximately 1/2 500 live female births. There is complete or partial absence of one of the two sex chromosomes, resulting in a genetic constellation of 45,X monosomy or 45,X/46,XX mosaic, respectively. In the present studies, using more accurate analysis with Fluorescence In Situ Hybridization (FISH), we investigated whether the international classification of the “genotype-phenotype correlation” should be different. TS women were compared with age-matched controls from the WHO MONICA study, carried out in Gothenburg, into cardiovascular risk factors and bone data. Stigmata were counted and balance and hearing were tested. Mosaics had fewer stigmata, no aortic dissection, were diagnosed 8 years later, had better balance and fine motor function and fewer cardiovascular risk factors compared with 45,X monosomy. The 45,X/46,XX mosaics were, thus, more similar to controls.

Mosaicism mitigated stigmata and the cardiovascular and fracture risk factor profile in TS.

Hypothyroidism and elevated liver enzymes are common in TS but no prospective studies have been performed. Thyroid function and liver enzymes were studied in TS patients during five years. The prevalence of hypothyroidism was 23% with an annual incidence of 3.2%, and the corresponding figures for elevated liver enzymes were 36% and 3.4%, respectively. Hypothyroidism was not associated with karyotype, family history or other metabolic factors but elevated thyroid peroxidase (TPO) antibodies were found in almost half of the TS cases with hypothyroidism. The most prevalently increased liver enzyme was gamma glutamyl transferase (GT) which was correlated with serum cholesterol, independently of obesity, waist/hip ratio and glucose level, but not with serum estradiol.

Every third TS woman developed hypothyroidism at five years and those with elevated TPO were at highest risk. Annual thyroid function control is mandatory. More than every second TS woman had elevated liver enzymes at five years. The elevated liver enzymes were benign. Estrogen replacement can be continued in TS.

Key words: Turner syndrome, chromosome, cardiovascular disease, body balance, fracture, hearing, hypothyroidism, liver

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